

CLAIMS

1. A population of microstructures comprising a permeable polymer shell,
5 wherein the standard variance in the volume of the microstructures is less than or equal to 10% of the mean, and wherein the diffusion characteristics of the polymer shell vary within the population of microstructures.
2. The population of microstructures of claim 1, wherein the diffusion
10 characteristics vary as a result of variable thickness of the shells of different microstructures in the population.
3. The population of microstructures of claim 2, wherein the thickness of the
15 shells varies continuously in the population.
4. The population of microstructures of claim 1, wherein the variance of the
diffusion characteristics of individual microstructures provides for a defined release
profile of an active agent encased in the microstructure.
- 20 5. The population of microstructures of claim 4, wherein the release profile is a sigmoidal summation profile.
6. The population of microstructures of claim 1, wherein the microstructures
25 are spherical.
7. The population of microstructures of claim 1, wherein the mean diameter of
the microstructures ranges from about 1 micron to about 100 microns.
8. The population of microstructures of claim 3, wherein the mean diameter of
30 the microstructures ranges from about 5 microns to about 50 microns.

9. The population of microstructures of claim 1, wherein the shell is a cationic cellulose derivative in an admixture with an anionic block copolymer.

5 10. The population of microstructures of claim 9, wherein the cellulose derivative is chitosan and the block copolymer is alginate.

11. A population of microstructures having a volume of less than or equal to about 10 nL comprising a cross-linked polymer, wherein the standard variance in the volume of the microstructures is less than or equal to 10% of the mean.

10 12. The population of microstructures of claim 11, wherein the microstructures are spherical.

13. The population of microstructures of claim 12, wherein the mean diameter of the microstructures ranges from about 1 micron to about 100 microns.

14. The population of microstructures of claim 13, wherein the mean diameter of the microstructures ranges from about 5 microns to about 50 microns.

20 15. The population of microstructures of claim 11, wherein the polymer is alginate cross-linked with calcium.

16. The population of microstructures of claim 11, further comprising a permeable polymer shell.

25 17. The population of microstructures of claim 16, wherein the shell is chitosan-alginate.

30 18. The population of microstructures of claim 17, wherein a thickness of the coating on each microstructure particle varies from other particles.

19. The population of microstructures of claim 17, wherein a thickness of the coating on each microstructure particle is substantially identical.

5 20. The population of microstructures of claim 11, further comprising a cell embedded in the cross-linked polymer.

21. A population of microstructures having a volume of less than or equal to about 10 nL comprising a permeable polymer shell, wherein the standard variance in the volume of the microstructures is less than or equal to 10% of the mean.

10 22. The population of microstructures of claim 11, further comprising a cell inside the microstructure.

15 23. The population of microstructures of claim 11, further comprising an active agent inside the microstructure.

20 24. A method of forming a population of microstructures, which method comprises introducing drops of a polymer solution into a receiving solution under conditions that permit cross-linking of the polymer in the receiving solution, wherein the drops have a standard variance in the volume that is less than or equal to 10% of the mean.

25 25. The method of claim 24, wherein the polymer solution is an aqueous solution and the receiving solution contains a hydrophobic component.

26. The method of claim 25, wherein the polymer solution is an alginate solution, and the organic solution is a mixture of a hydrocarbon and an alcohol comprising a calcium salt in a concentration sufficient to cross-link the alginate.

27. The method of claim 24, wherein the polymer solution is an aqueous solution comprising cells, wherein each drop comprises on average a single cell, and the receiving solution is also an aqueous solution.

5 28. The method of claim 27, wherein the polymer solution is an alginate solution, and the receiving solution comprises a calcium salt in a concentration sufficient to cross-link the alginate.

10 29. The method of claim 24, further comprising contacting the microstructure with a polymer, wherein the polymer interacts with and stabilizes the cross-linked polymer.

30. The method of claim 29, wherein the polymer is chitosan.

15 31. The method of claim 29, further comprising dissolving the cross-linked polymer cross-links.

32. The method of claim 31, wherein the polymer is alginate cross-linked with calcium contacted with a calcium chelating agent.

20 33. The method of claim 32, wherein the calcium chelating agent is sodium citrate.

25 34. The method of claim 27, further comprising contacting the microstructure with a permeable polymer, wherein the polymer interacts with and stabilizes the cross-linked polymer.

35. The method of claim 34, wherein the polymer is chitosan.

30 36. The method of claim 34, further comprising dissolving the polymer cross-links.

37. The method of claim 36, wherein the polymer is alginate cross-linked with calcium contacted with a calcium chelating agent.

5 38. The method of claim 24, wherein the drops are formed in a drop-forming apparatus comprising an orifice, a polymer solution supply reservoir, an activation element, and a controller.

10 39. The method of claim 38, wherein the apparatus is a modified inkjet printer cartridge.

40. The method of claim 38, wherein the apparatus employs inkjet printer cartridge components modified for forming polymer solution drops.

15 41. The method of claim 29, further comprising loading the microstructure with an active ingredient.

42. The method of claim 41, wherein the loading comprises gradient diffusion.

20 43. A drop-forming apparatus comprising a plurality of orifices of uniform size spaced far enough apart so that drops ejected from the orifices do not combine, a reservoir in liquid communication with the plurality of orifices, and an activation means for ejecting drops from each orifice.

25 44. The apparatus of claim 43 wherein the orifices are formed in metal foil.

45. The apparatus of claim 44, wherein the metal foil is gold foil.

30 46. The apparatus of claim 43, wherein each orifice has a diameter of about 30 microns.

47. The apparatus of claim 43, wherein the distance between each orifice is an order of magnitude greater than the diameter of each orifice.

5 48. The apparatus of claim 43, wherein the activation means comprises a controller and an activation element.

49. The apparatus of claim 48, wherein controller is an amplified constant pulse generator and the activation element is a resistor.

10 50. A population of microstructures comprising alginate cross-linked with calcium, wherein the standard variance in the volume of the microstructures is less than or equal to 5% of the mean.

15 51. The population of microstructures of claim 50, further comprising a chitosan-alginate shell.

52. The population of microstructures of claim 51, wherein a thickness of the chitosan shell on each microstructure particle varies from other particles.

20 53. The population of microstructures of claim 52, wherein the thickness of the chitosan shell varies continuously in the population.

25 54. The population of microstructures of claim 52, wherein the variance of the shell thickness of individual microstructures provides for a defined release profile of an active agent encased in the microstructure.

55. The population of microstructures of claim 54, wherein the release profile is a sigmoidal summation profile.

30 56. The population of microstructures of claim 51, wherein a thickness of the chitosan coating on each microstructure particle is substantially identical.

57. The population of microstructures of claim 51, further comprising an active agent.

5 58. The population of microstructures of claim 50, further comprising a cell in the alginate.

59. A population of microstructures comprising a permeable chitosan shell, wherein the standard variance in the volume of the microstructures is less than or
10 equal to 10% of the mean.

60. The population of microstructures of claim 59, further comprising a cell inside the microstructure.

15 61. The population of microstructures of claim 59, further comprising an active agent inside the microstructure.